

containing tiny, electron-dense granules and sometimes possessing internal cavities and external membranes (Figure 6.15). They tentatively identified the particles as the lysosomes (Novikoff, Beaufay, & de Duve, 1956). Novikoff (1961) went on to develop light and electron microscope stains for acid phosphatase and used the presence of a membrane and the positive indication of acid phosphatase as evidence for lysosomes, noting that they often differed substantially in size in different cell types.⁴⁶ Treating intracellular digestion as the defining function of lysosomes, Novikoff proposed differentiating lysosomes according to the types of exogenous or endogenous material the lysosome would digest.

Working at the State University of New York College of Medicine in Brooklyn during the same period as de Duve, Werner Straus identified droplets in the proximal tubule of the kidney that stored and broke down reabsorbed proteins. He determined that they possessed an unusually high concentration of acid phosphatase (Straus, 1954). After learning of the other enzymes de Duve associated with lysosomes, Straus (1956) determined that they were present in his droplets as well. Straus's research drew attention to the connection between lysosomes and the digestion of material brought into the cell as well as breakdown products of the cell itself. This idea of the function of the lysosome was further developed by de Duve (1958):

Our working hypothesis will therefore be that lysosomes are involved in processes of acid hydrolysis. These may comprise: digestion of foreign material, engulfed by pinocytosis, athrocytosis or phagocytosis; physiologic autolysis, as presumably occurs to some extent in all tissues, and particularly as part of the more specialized processes of involution, metamorphosis, holocrine secretion, etc; pathological autolysis or necrosis. (p. 146)

Initially it was difficult to identify lysosomes in other cells due to the variability in their shape and size, causing de Duve to be reluctant to generalize the lysosome concept. Once their role in cellular digestion was understood, this variability made sense: "This polymorphism of the lysosomes is now perfectly understandable: their digestive activity causes them to be filled with a variety of substances and objects in an advanced state of disintegration,

⁴⁶ Regarding this, de Duve (1969, p. 16) commented, "I must confess that Novikoff, who pioneered this field with untiring energy, received little encouragement on my part. I objected strongly to what I considered a misappropriation of the word *lysosome*, which in my own copyrighted version implied the simultaneous presence of several acid hydrolases, and which he was now using to designate any structure giving a positive reaction for a single such enzyme." Novikoff, however, expressly agreed with de Duve that *intracellular digestion* was the defining function of lysosomes (Novikoff & Holtzman, 1970).